

We Claim:

1. An isolated mutant BRCA1 gene or polynucleotide fragment thereof containing a mutation site, or a polynucleotide complementary to said gene or said fragment, having an in-frame stop codon before codon 1863, with the proviso that the mutation site not be one defined by TABLE 1.
2. An isolated mutant BRCA1 gene, a polynucleotide fragment of said mutant BRCA1 gene, or a complementary polynucleotide to said mutant BRCA1 gene or said fragment, according to claim 1, containing a truncating mutation and forming a stop codon as defined in TABLES 3-7, wherein the mutant BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.
3. An isolated mutant BRCA1 gene, a polynucleotide fragment of said mutant BRCA1 gene or a complementary polynucleotide to said mutant BRCA1 gene or said fragment according to claim 1, containing a truncating mutation and having the sequence 5' R1-R2-R3 3'; where

R1 is a wild type BRCA1 DNA sequence from nucleotide number 120 to X, R2 is TAA, TAG or TGA, and R3 is a wild type BRCA1 DNA sequence from nucleotide number X+4 to 5711 and where X = 123 to 5710; or

R1 is a wild type BRCA1 DNA sequence from nucleotide number 120 to X, R2 is zero nucleotides, and R3 is the wild type BRCA1 DNA sequence from nucleotides X+Y+1 to 5711, where Y is an integer of $3n+1$ or $3n+2$ where $n=0$ to 1861 and where X = 123 to 5707; or

R1 is a wild type BRCA1 DNA sequence from nucleotide number 120 to X, R2 is Y nucleotides of any sequence, and R3 contains the wild type BRCA1 DNA sequence of nucleotide number X+1 to 5711, where Y is $3n+1$ or $3n+2$ where n is an integer of zero or greater, and where X = 123 to 5707;

wherein the BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein, with the proviso that the mutation not be one defined by TABLE 1.

4. An isolated mutant BRCA1 gene or a polynucleotide fragment thereof, or a polynucleotide complementary to said mutant BRCA1 gene or said fragment according to claim 1, containing a truncating mutation site and capable of specifically hybridizing to an oligonucleotide probe being at least 12 nucleotides in length and having the sequence 5' R1-R2-R3 3'; where either

R1 contains at its 3' end three nucleotides complementary to codon X-1 of the wild-type BRCA1 gene; R2 is complementary to TAG, TAA or TGA, and R3 contains at its 5' end three nucleotides complementary to codon X+1 of the wild type BRCA1 gene, where X = 2 to 1862; or

R1 contains at its 3' end three nucleotides complementary to nucleotide numbers X-2 to X of the wild-type BRCA1 gene, R2 is an oligonucleotide having Y nucleotides of any sequence, R3 contains at its 5' end three nucleotides complementary to nucleotide numbers X+1 to X+3 of the wild type BRCA1 gene, where Y is an integer greater than zero and is not 3 or a multiple of 3, where X = 122 to 5707; or

R1 contains at its 3' end three nucleotides complementary to nucleotide numbers X-2 to X of the wild-type BRCA1 gene, R2 = zero, R3 contains at its 5' end three nucleotides complementary to nucleotide numbers X+1+Y of the wild type BRCA1 DNA sequence, where Y = 1 to 5582 but is not 3 or a multiple of 3 and where X = 122 to 5706;

wherein the oligonucleotide probe is unable to specifically hybridize to the wild-type BRCA1 gene; and with the proviso that the mutation not be one defined by TABLE 1.

5. A mutant BRCA1 gene or a polynucleotide fragment thereof, or a polynucleotide complementary to said mutant BRCA1 gene or said fragment according to claim 1, containing a premature stop codon and incapable of expressing a complete BRCA1 protein;

wherein said mutant BRCA1 gene contains a mutation resulting from a substituted nucleotide in the naturally occurring (wild-type) sequence so that an in-frame stop codon is formed at any of codon numbers 2-1863; or

inserted or deleted $3n+1$ or $3n+2$ nucleotides, where n is an integer of 0 or greater, causing a frame shift mutation in the naturally occurring (wild-type) sequence so that an in-frame stop codon is formed at any of codon numbers 2-1863;

wherein a mutant BRCA1 protein expressed from said mutant BRCA1 gene lacks full biological activity of naturally occurring (wild type) BRCA1 protein; and

with the proviso that the mutation is not one of the mutations listed in TABLE 1.

6. A method for detecting a mutation in a sample containing a mutant BRCA1 gene according to claim 1, comprising:

- a) amplifying at least a fragment of sample BRCA1 gene;
- b) determining the sequence of said at least a fragment of the sample BRCA1 gene;
and
- c) comparing the sequence obtained with a wild-type BRCA1 sequence;

wherein the presence of the sequence of said mutation in said sample BRCA1 gene indicates the presence of a mutation in the sample.

7. A method for detecting a mutation in a sample containing a BRCA1 gene comprising:

- a) amplifying at least a fragment of sample BRCA1 gene;
- b) determining the sequence of said at least a fragment of sample BRCA1 gene; and
- c) comparing the sequence obtained with one or more sequences of mutant BRCA1 genes according to claim 1;

wherein the presence of a sequence of said mutant BRCA1 gene indicates the presence of a mutation in the sample.

8. A method for detecting a mutation in a BRCA1 gene comprising:

- a) obtaining a BRCA1 protein expressed by a BRCA1 gene according to claim 1;
and
- b) determining the relative molecular weight of said BRCA1 protein compared to wild type BRCA1 protein;

- c) wherein the presence of said BRCA1 protein having a molecular weight less than that of wild-type BRCA1 protein indicates the presence of a mutation in the BRCA1 gene.

9. An oligonucleotide capable of specifically hybridizing to either:

- a) a DNA containing a mutant BRCA1 as defined in claim 1, or a DNA having a sequence complementary thereto; or
- b) a DNA containing a wild-type BRCA1 sequence at a mutation site other than defined by TABLE 1, or a DNA having a sequence complementary thereto;

but not both a) and b).

10. A plurality of oligonucleotides comprising at least one oligonucleotide according to claim 9 and at least one additional oligonucleotide capable of specifically hybridizing to the wild-type BRCA1 gene or its complement.

11. A chip array having "n" elements for performing allele specific sequence-based techniques using the oligonucleotide probes comprising, a solid phase chip and a plurality of oligonucleotides of claim 10 having "n" different nucleotide sequences, wherein "n" is an integer greater than one;

wherein said oligonucleotides are bound to said solid phase chip in a manner which permits said oligonucleotides to effectively hybridize to complementary oligonucleotides or polynucleotides;

wherein oligonucleotides having different nucleotide sequences are bound to said solid phase chip at different locations so that a particular location on said solid phase chip exclusively binds oligonucleotides having a specific nucleotide sequence; and

wherein at least one oligonucleotide is capable of specifically hybridizing to a mutant BRCA1 gene having a truncating mutation as defined by TABLES 3-7 or a DNA complementary thereto, with the proviso that the mutation not be one defined by TABLE 1, wherein the BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.

12. A method for detecting the presence or absence of a BRCA1 gene mutation in a sample DNA comprising, specifically hybridizing sample DNA with an oligonucleotide according to claim 9 under stringent conditions and determining whether said oligonucleotide specifically hybridizes to said sample DNA.
13. A method for determining therapy for an individual having a tumor comprising:
 - a) obtaining a DNA containing biological sample from the individual having a tumor;
 - b) determining whether the DNA contains a mutant BRCA1 gene according to claim 1, or a DNA complementary thereto; and
 - c) determining appropriate therapy based on the presence or absence of said mutant BRCA1 gene;

wherein the BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.

14. A method for determining whether to begin diagnostic or prophylactic treatment for an individual comprising:
 - a) obtaining a DNA containing biological sample from the individual;

- b) determining whether the DNA contains a mutant BRCA1 gene according to claim 1; and
- c) determining appropriate diagnostic or prophylactic treatment based on the presence or absence of said mutant BRCA1 gene;

wherein the mutant BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.

- 15. A method for treating a condition associated with a mutant BRCA1 gene comprising administering biologically active BRCA1 protein to a patient with a condition associated with a mutant BRCA1 gene wherein said patient contains cells having a mutant BRCA1 gene according to claim 1, wherein the BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.
- 16. A method for preventing a condition associated with a mutant BRCA1 gene comprising administering biologically active BRCA1 protein to a patient with a cancer wherein said patient contains cells having a truncating BRCA1 gene mutation according to claim 1, wherein the BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.
- 17. A method for determining appropriate gene therapy for an individual comprising detecting the presence of a mutant BRCA1 gene according to claim 1, in cells from the individual and administering a DNA containing biologically active BRCA1 gene to the individual, wherein the mutant BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.
- 18. A method for detecting a mutation in a sample containing a mutant BRCA1 gene according to claim 2, comprising:

- a) amplifying at least a fragment of sample BRCA1 gene;
- b) determining the sequence of said at least a fragment of sample BRCA1 gene; and
- c) comparing the sequence obtained with a wild-type BRCA1 sequence;

wherein the presence of the sequence of said mutant BRCA1 gene indicates the presence of a mutation in the sample.

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19. A method for detecting a mutation in a sample containing a BRCA1 gene comprising:

- a) amplifying at least a fragment of sample BRCA1 gene;
- b) determining the sequence of said at least a fragment of sample BRCA1 gene; and
- c) comparing the sequence obtained with one or more of mutant BRCA1 genes according to claim 2;

wherein the presence of a sequence of said mutant BRCA1 gene indicates the presence of a mutation in the sample.

20. A method for detecting a mutation in a BRCA1 gene comprising:

- a) obtaining a BRCA1 protein expressed by a BRCA1 gene according to claim 2;
and
- b) determining the relative molecular weight of said BRCA1 protein compared to wild type BRCA1 protein;

wherein the presence of said BRCA1 protein having a molecular weight less than that of wild-type BRCA1 protein indicates the presence of a mutation in the BRCA1 gene.

21. An oligonucleotide capable of specifically hybridizing to either:
- a) a DNA containing a mutant BRCA1 as defined in claim 2, or a DNA having a sequence complementary thereto; or
 - b) a DNA containing a wild-type BRCA1 sequence at a mutation site other than defined by TABLE 1, or a DNA having a sequence complementary thereto;

but not both a) and b).

22. A plurality of oligonucleotides comprising at least one oligonucleotide according to claim 21 and at least one additional oligonucleotide capable of specifically hybridizing to the wild-type BRCA1 gene or its complement.

23. A chip array having "n" elements for performing allele specific sequence-based techniques using the oligonucleotide probes comprising a solid phase chip and a plurality of oligonucleotides of claim 22 having "n" different nucleotide sequences, wherein "n" is an integer greater than two;

wherein said oligonucleotides are bound to said solid phase chip in a manner which permits said oligonucleotides to effectively hybridize to complementary oligonucleotides or polynucleotides;

wherein oligonucleotides having different nucleotide sequences are bound to said solid phase chip at different locations so that a particular location on said solid phase chip exclusively binds oligonucleotides having a specific nucleotide sequence; and

wherein at least one oligonucleotide is capable of specifically hybridizing to a mutant BRCA1 gene having a truncating mutation as defined by TABLES 3-7 or a DNA complementary thereto, with the proviso that the mutation not be one defined by TABLE

1, wherein the BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.

24. A method for detecting the presence or absence of a BRCA1 gene mutation in a sample DNA comprising specifically hybridizing sample DNA with an oligonucleotide according to claim 21 under stringent conditions and determining whether said oligonucleotide specifically hybridizes to said sample DNA.

25. A method for determining therapy for an individual having a tumor comprising obtaining a DNA containing biological sample from the individual having a tumor, determining whether the DNA contains a mutant BRCA1 gene according to claim 2, or a DNA complementary thereto, and determining appropriate therapy based on the presence or absence of said mutant BRCA1 gene, wherein the BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.

26. A method for determining whether to begin diagnostic or prophylactic treatment for an individual comprising:

- a) taking a DNA containing biological sample from the individual;
- b) determining whether the DNA contains a mutant BRCA1 gene according to claim 2; and
- c) determining appropriate diagnostic or prophylactic treatment based on the presence or absence of said mutant BRCA1 gene;

wherein the mutant BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.

27. A method for treating a condition associated with a mutant BRCA1 gene comprising, administering biologically active BRCA1 protein to a patient with a condition associated with a mutant BRCA1 gene wherein said patient contains cells having a mutant BRCA1 gene according to claim 2, wherein the BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.
28. A method for preventing a condition associated with a mutant BRCA1 gene comprising, administering biologically active BRCA1 protein to a patient with a cancer wherein said patient contains cells having a truncating BRCA1 gene mutation according to claim 2, wherein the BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.
29. A method for determining appropriate gene therapy for an individual comprising, detecting the presence of a mutant BRCA1 gene according to claim 2, in cells from the individual and administering a DNA containing biologically active BRCA1 gene to the individual, wherein the mutant BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.
30. A method for detecting a mutation in a sample containing a mutant BRCA1 gene according to claim 3, comprising:
- a) amplifying at least a fragment of sample BRCA1 gene;
 - b) determining the sequence of said at least a fragment of sample BRCA1 gene; and
 - c) comparing the sequence obtained with a wild-type BRCA1 sequence;
- wherein the presence of the sequence of said mutant BRCA1 gene indicates the presence of a mutation in the sample.

31. A method for detecting a mutation in a sample containing a BRCA1 gene comprising:
- a) amplifying at least a fragment of sample BRCA1 gene;
 - b) determining the sequence of said at least a fragment of sample BRCA1 gene; and
 - c) comparing the sequence obtained with one or more of mutant BRCA1 genes according to claim 3;

wherein the presence of a sequence of said mutant BRCA1 gene indicates the presence of a mutation in the sample.

32. A method for detecting a mutation in a BRCA1 gene comprising, obtaining a BRCA1 protein expressed by a BRCA1 gene according to claim 3, and determining the relative molecular weight of said BRCA1 protein compared to wild type BRCA1 protein, wherein the presence of said BRCA1 protein having a molecular weight less than that of wild-type BRCA1 protein indicates the presence of a mutation in the BRCA1 gene.

33. An oligonucleotide capable of specifically hybridizing to either:
- a) a DNA containing a mutant BRCA1 as defined in claim 3, or a DNA having a sequence complementary thereto; or
 - b) a DNA containing a wild-type BRCA1 sequence at a mutation site other than defined by TABLE 1, or a DNA having a sequence complementary thereto;

but not both a) and b).

34. A plurality of oligonucleotides comprising at least one oligonucleotide according to claim 33 and at least one additional oligonucleotide capable of specifically hybridizing to the wild-type BRCA1 gene or its complement.

5 35. A chip array having "n" elements for performing allele specific sequence-based techniques using oligonucleotide probes comprising, a solid phase chip and a plurality of oligonucleotides of claim 34 having "n" different nucleotide sequences, wherein "n" is an integer greater than two;

wherein said oligonucleotides are bound to said solid phase chip in a manner which permits said oligonucleotides to effectively hybridize to complementary oligonucleotides or polynucleotides;

wherein oligonucleotides having different nucleotide sequences are bound to said solid phase chip at different locations so that a particular location on said solid phase chip exclusively binds oligonucleotides having a specific nucleotide sequence; and

15 wherein at least one oligonucleotide is capable of specifically hybridizing to a mutant BRCA1 gene having a truncating mutation as defined by TABLES 3-7 or a DNA complementary thereto, with the proviso that the mutation not be one defined by TABLE 1, wherein the BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.

20 36. A method for detecting the presence or absence of a BRCA1 gene mutation in a sample DNA comprising, specifically hybridizing sample DNA with an oligonucleotide according to claim 33 under stringent conditions, and determining whether said oligonucleotide specifically hybridizes to said sample DNA.

37. A method for determining therapy for an individual having a tumor comprising;

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- a) obtaining a DNA containing biological sample from the individual having a tumor;
 - b) determining whether the DNA contains a mutant BRCA1 gene according to claim 3, or a DNA complementary thereto; and
 - c) determining appropriate therapy based on the presence or absence of said mutant BRCA1 gene;

wherein the BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.

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38. A method for determining whether to begin diagnostic or prophylactic treatment for an individual comprising:

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- a) obtaining a DNA containing biological sample from the individual;
 - b) determining whether the DNA contains a mutant BRCA1 gene according to claim 3; and
 - c) determining appropriate diagnostic or prophylactic treatment based on the presence or absence of said mutant BRCA1 gene;

wherein the mutant BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.

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39. A method for treating a condition associated with a mutant BRCA1 gene comprising, administering biologically active BRCA1 protein to a patient with a condition associated with a mutant BRCA1 gene wherein said patient contains cells having a mutant BRCA1

gene according to claim 3, wherein the BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.

5 40. A method for preventing a condition associated with a mutant BRCA1 gene comprising, administering biologically active BRCA1 protein to a patient with a cancer wherein said patient contains cells having a truncating BRCA1 gene mutation according to claim 3, wherein the BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.

41. A method for determining appropriate gene therapy for an individual comprising, detecting the presence of a mutant BRCA1 gene according to claim 3 in cells from the individual and administering a DNA containing biologically active BRCA1 gene to the individual, wherein the mutant BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.

42. A method for detecting a mutation in a sample containing a mutant BRCA1 gene according to claim 4, comprising:

- 15 a) amplifying at least a fragment of sample BRCA1 gene;
- b) determining the sequence of said at least a fragment of sample BRCA1 gene; and
- c) comparing the sequence obtained with a wild-type BRCA1 sequence;

wherein the presence of the sequence of said mutant BRCA1 gene indicates the presence of a mutation in the sample.

20 43. A method for detecting a mutation in a sample containing a BRCA1 gene comprising:

- a) amplifying at least a fragment of sample BRCA1 gene;

- b) determining the sequence of said at least a fragment of sample BRCA1 gene; and
- c) comparing the sequence obtained with one or more of mutant BRCA1 genes according to claim 4;

wherein the presence of a sequence of said mutant BRCA1 gene indicates the presence of a mutation in the sample.

44. A method for detecting a mutation in a BRCA1 gene comprising, obtaining a BRCA1 protein expressed by a BRCA1 gene according to claim 4, and determining the relative molecular weight of said BRCA1 protein compared to wild type BRCA1 protein, wherein the presence of said BRCA1 protein having a molecular weight less than that of wild-type BRCA1 protein indicates the presence of a mutation in the BRCA1 gene.

45. An oligonucleotide capable of specifically hybridizing to either:

- a) a DNA containing a mutant BRCA1 as defined in claim 4, or a DNA having a sequence complementary thereto; or
- b) a DNA containing a wild-type BRCA1 sequence at a mutation site other than defined by TABLE 1, or a DNA having a sequence complementary thereto;

but not both a) and b).

46. A plurality of oligonucleotides comprising at least one oligonucleotide according to claim 45 and at least one additional oligonucleotide capable of specifically hybridizing to the wild-type BRCA1 gene or its complement.

47. A chip array having "n" elements for performing allele specific sequence-based techniques using the oligonucleotide probes comprising, a solid phase chip and a plurality

of oligonucleotides of claim 46 having "n" different nucleotide sequences, wherein "n" is an integer greater than two;

wherein said oligonucleotides are bound to said solid phase chip in a manner which permits said oligonucleotides to effectively hybridize to complementary oligonucleotides or polynucleotides;

wherein oligonucleotides having different nucleotide sequences are bound to said solid phase chip at different locations so that a particular location on said solid phase chip exclusively binds oligonucleotides having a specific nucleotide sequence; and

wherein at least one oligonucleotide is capable of specifically hybridizing to a mutant BRCA1 gene having a truncating mutation as defined by TABLES 3-7 or a DNA complementary thereto, with the proviso that the mutation not be one defined by TABLE 1, wherein the BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.

48. A method for detecting the presence or absence of a BRCA1 gene mutation in a sample DNA comprising, specifically hybridizing sample DNA with an oligonucleotide according to claim 45 under stringent conditions, determining whether said oligonucleotide specifically hybridizes to said sample DNA.

49. A method for determining therapy for an individual having a tumor comprising;

- a) obtaining a DNA containing biological sample from the individual having a tumor;
- b) determining whether the DNA contains a mutant BRCA1 gene according to claim 4, or a DNA complementary thereto; and

- c) determining appropriate therapy based on the presence or absence of said mutant BRCA1 gene;

wherein the BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.

- 5 50. A method for determining whether to begin diagnostic or prophylactic treatment for an individual comprising:

- a) taking a DNA containing biological sample from the individual;
- b) determining whether the DNA contains a mutant BRCA1 gene according to claim 4; and
- c) determining appropriate diagnostic or prophylactic treatment based on the presence or absence of said mutant BRCA1 gene;

wherein the mutant BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.

- 15 51. A method for treating a condition associated with a mutant BRCA1 gene comprising, administering biologically active BRCA1 protein to a patient with a condition associated with a mutant BRCA1 gene wherein said patient contains cells having a mutant BRCA1 gene according to claim 4, wherein the BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.

- 20 52. A method for preventing a condition associated with a mutant BRCA1 gene comprising, administering biologically active BRCA1 protein to a patient with a cancer, wherein said patient contains cells having a truncating BRCA1 gene mutation according to claim 4,

wherein the BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.

53. A method for determining appropriate gene therapy for an individual comprising, detecting the presence of a mutant BRCA1 gene according to claim 4 in cells from the individual, and administering a DNA containing biologically active BRCA1 gene to the individual, wherein the mutant BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.
54. A method for detecting a mutation in a sample containing a mutant BRCA1 gene according to claim 5, comprising, amplifying at least a fragment of said BRCA1 gene, determining the sequence of said at least a fragment of said BRCA1 gene, and comparing the sequence obtained with a wild-type BRCA1 sequence, wherein the presence of the sequence of said mutant BRCA1 gene indicates the presence of a mutation in the sample.
55. A method for detecting a mutation in a sample containing a BRCA1 gene comprising, amplifying at least a fragment of said BRCA1 gene, determining the sequence of said at least a fragment of said BRCA1 gene, and comparing the sequence obtained with one or more of mutant BRCA1 genes according to claim 5, wherein the presence of a sequence of said mutant BRCA1 gene indicates the presence of a mutation in the sample.
56. A method for detecting a mutation in a BRCA1 gene comprising, obtaining a BRCA1 protein expressed by a BRCA1 gene according to claim 5, and determining the relative molecular weight of said BRCA1 protein compared to wild type BRCA1 protein, wherein the presence of said BRCA1 protein having a molecular weight less than that of wild-type BRCA1 protein indicates the presence of a mutation in the BRCA1 gene.
57. An oligonucleotide capable of specifically hybridizing to either:

- a) a DNA containing a mutant BRCA1 as defined in claim 5, or a DNA having a sequence complementary thereto; or
- b) a DNA containing a wild-type BRCA1 sequence at a mutation site other than defined by TABLE 1, or a DNA having a sequence complementary thereto;

but not both a) and b).

58. A plurality of oligonucleotides comprising at least one oligonucleotide according to claim 57 and at least one additional oligonucleotide capable of specifically hybridizing to the wild-type BRCA1 gene or its complement.

59. A chip array having "n" elements for performing allele specific sequence-based techniques using the oligonucleotide probes comprising, a solid phase chip and a plurality of oligonucleotides of claim 58 having "n" different nucleotide sequences, wherein "n" is an integer greater than two;

wherein said oligonucleotides are bound to said solid phase chip in a manner which permits said oligonucleotides to effectively hybridize to complementary oligonucleotides or polynucleotides;

wherein oligonucleotides having different nucleotide sequences are bound to said solid phase chip at different locations so that a particular location on said solid phase chip exclusively binds oligonucleotides having a specific nucleotide sequence; and

wherein at least one oligonucleotide is capable of specifically hybridizing to a mutant BRCA1 gene having a truncating mutation as defined by TABLES 3-7 or a DNA complementary thereto, with the proviso that the mutation not be one defined by TABLE

1, wherein the BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.

5 60. A method for detecting the presence or absence of a BRCA1 gene mutation in a sample DNA comprising, specifically hybridizing sample DNA with an oligonucleotide according to claim 57 under stringent conditions, and determining whether said oligonucleotide specifically hybridizes to said sample DNA.

61. A method for determining therapy for an individual having a tumor comprising;

- a) obtaining a DNA containing biological sample from the individual having a tumor;
- b) determining whether the DNA contains a mutant BRCA1 gene according to claim 5, or a DNA complementary thereto; and
- c) determining appropriate therapy based on the presence or absence of said mutant BRCA1 gene;

15 wherein the BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.

20 62. A method for determining whether to begin diagnostic or prophylactic treatment for an individual comprising, taking a DNA containing biological sample from the individual, determining whether the DNA contains a mutant BRCA1 gene according to claim 5, and determining appropriate diagnostic or prophylactic treatment based on the presence or absence of said mutant BRCA1 gene, wherein the mutant BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.

63. A method for treating a condition associated with a mutant BRCA1 gene comprising, administering biologically active BRCA1 protein to a patient with a condition associated with a mutant BRCA1 gene, wherein said patient contains cells having a mutant BRCA1 gene according to claim 5, wherein the BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.
64. A method for preventing a condition associated with a mutant BRCA1 gene comprising, administering biologically active BRCA1 protein to a patient with a cancer, wherein said patient contains cells having a truncating BRCA1 gene mutation according to claim 5, wherein the BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.
65. A method for determining appropriate gene therapy for an individual comprising, detecting the presence of a mutant BRCA1 gene according to claim 5 in cells from the individual, and administering a DNA containing biologically active BRCA1 gene to the individual, wherein the mutant BRCA1 gene codes for a truncated BRCA1 protein which lacks full biological activity of wild-type BRCA1 protein.
66. An isolated mutant BRCA1 gene according to claim 1, capable of expressing a truncated BRCA1 protein of less than 1854 amino acids.